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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/739,933	12/18/2000	James Steven Reid	07306-021001	4882

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EXAMINER	
TURNER, SHARON L	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/05/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/739,933	Fallon et al
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 5-10-02

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-62 is/are pending in the applica

4a) Of the above, claim(s) 9-15, 17-19, 21-26, 28-32, and 34-62 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-8, 16, 20, 27, and 33 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 1-62 are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on 12-18-00 is/are a☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b) ☐ Some* c) ☐None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-62 are pending.

Election/Restriction

2. Applicant's election with traverse of Group I, claims 1-8, 16, 20, 27 and 33 in part to the extent drawn to TGF-α, second compound that inhibits a naturally occurring signal that inhibits migration and neurodegenerative disease, in Paper No. 13 is acknowledged. The traversal is on the ground(s) that the search and examination of the different inventions and species would not be burdensome or unreasonable. This is not found persuasive because the methods are distinct as they are comprised of different steps, utilize different reagents and achieve distinct results as claimed. Thus, a search for one of the methods or species would not be co-extensive with a search for any other method or species.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 9-15, 17-19, 21-26, 28-32 and 34-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13. It is noted that withdrawn claims 9-15, 21-26, and 28-32 are drawn to divergent species not clearly directed to the elected subject matter. These claims differ from applicant's statement of claims readable on the invention.

MJK

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8, 20, 27 and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims recite contacting with a compound that binds to an epidermal growth factor (EGF)/ErbB family receptor, which attracts glial progenitor cells or progeny thereof and which stimulates differentiation of the glial progenitor cell or progeny thereof. Claim 27 recites a second compound that is capable of inhibiting a naturally occurring signal that would otherwise inhibit migration of the glial progenitor cell or its progeny. While the disclosure teaches that Transforming growth factor alpha (TGF-α) is a molecule which binds EGF receptor, the recitation of alternative ill described molecules which maintain such functional activities as noted above merely represents a functional recitation of multiple distinct classes of molecules which are not structurally described but which are encompassed by the claims. While the disclosure provides written description of TGF-α, the disclosure fails to provide a written description supportive of all means of achieving such function, but only those in possession by applicant at the time of the invention, see MPEP 2164.08(a). Thus, the written description provided by the disclosure is not commensurate with that claimed and the artisan cannot conceive based on the

single species the genus of molecules claimed. Moreover, there appears to be no single embodiment disclosed for the recitation of the second compound in claim 27.

A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

Here, the description for the first compound provides only a single species and no description of the structural requirements of the molecules, falling within the scope of the genus,

or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. However, it is noted that no single species is recognized for the second compound as noted in claim 27. The artisan readily recognizes the unpredictability in the art in determining structure function relationships of peptides and peptide families even amongst highly conserved variants, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000. Given the unpredictability of homology comparisons, and the fact that the specification fails to provide objective evidence any additional peptide sequences that are indeed species of the claimed genus', it cannot be established that a representative number of species have been disclosed to support the genus' molecules claim. Thus, instant claims lack adequate written description support for the first and second compounds of the claims.

6. Claims 1-8, 20, 27 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for TGF-α binding to the EGF receptor, does not reasonably provide enablement for the generic recitation of all compounds which bind to the EGF receptor to attract a glial progenitor cell or progeny thereof or to stimulate differentiation as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the

unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

The claims are akin to a single means claim, i.e., where a means recitation does not appear in combination with another recited element of means. In the instant case the claim does recite an element of means. However, the element of means is described only as a compound which binds the EGF/erbB family receptor. While the specification teaches that TGF-α is such a polypeptide, the disclosure falls short of describing any other structural molecules which binds EGF receptor to produce the noted effects. Thus, it seems that the claim is subject to an undue breadth rejection under 35 USC 112, first paragraph. In particular MPEP 2164.08(a) and In re Hyatt, 708F.2d 712, 714, 715 (218 USPQ 195, 197) (Fed. Cir. 1983) describe where a single means claim which covered every conceivable means for achieving the stated purpose was held non-enabling for the scope of the claim because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor.

It is further noted that applicant's disclosure fails to teach the structural and functional relationship recited, i.e., the compound(s) able to produce the required attraction of glial progenitor cells or progeny thereof and to stimulate differentiation of glial progenitor cells or progeny thereof as claimed. Moreover, there is no single embodiment recognized for the second

compound as claimed in claim 27. No molecule with the noted properties is disclosed. In particular as noted by Kudlow et al., J. Biol Chem 259(19):11895-900, 1984 and Carpenter et al., PNAS 80(18):5627-30, 1983 binding of the EGF receptor fails to ensure that normal effects are produced as exemplified by two EGF receptor antibodies which bind but fail to activate receptor properties in different systems. The skilled artisan thus would have reason to doubt that merely binding the receptor is sufficient to produce the claimed effects in neural progenitor cells.

Moreover as directed to functional fragments of TGF-α, the specification fails to teach the required structural identity of such molecules which are capable of not only attracting progenitor cells but producing differentiation. There is no guidance as to which portions of the molecule are required to be retained to maintain the functional activity. The skilled artisan readily recognizes the unpredictability in the art of determining structure function relationships even amongst highly homologous family members, see in particular Skolnick et al., Trends in Biotech., 18(1):34-39, 2000, Abstract and Box 2.

Thus, for the aforementioned reasons the skilled artisan would not be able make and use the claimed invention, commensurate in scope with the claims, without further undue experimentation to discover those molecules of first and second compounds capable of producing the claimed effects.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: those steps which link the in vitro administration of the compound to the method as claimed in claim 1. It is noted that the administration is required to be at the a site in a CNS tissue as claimed in claim 1. Thus, there appears to be a gap between the steps and the claim lacks clear antecedent basis for the locale of administration which is a glial tissue culture comprising a glial progenitor cell. Applicants should clarify how claim 20 is deemed to further limit claim 1. Perhaps applicants wish to recite, "wherein the CNS tissue is in tissue culture," as for example in hippocampal explants. Clarification is required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in

> section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
>
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 1-7, 16 and 33 are rejected under 35 U.S.C. 102(a) as being anticipated by Reid et al., Radial Migration of Subependymal Cells in the Adult Rodent Forebrain, Abstract 8-7-97, Department of Anatomy and Neurobiology, University of California, Irvine CA 92717.

It is noted as disclosed and recognized in the art that TGF-α binds the EGF receptor, see in particular p. 2 and Todaro et al., PNAS 77:5258-62, 1980.

Reid et al., teaches striatal infusion of TGF-α in lesioned dopaminergic nigrostriatal pathway, a model of Parkinson's Disease based upon dopamine cell denervation (causing damage to neuronal cells). Reid et al., teaches that the infused TGF-α induces cells in the subependymal zone to proliferate and migrate radially into the overlying striatum. As the treatment involves administration of TGF-α to the brain and results in the contact of TGF-α, a compound that binds the EGF receptor, with neural progenitor cells within the striatum and subependymal zone, the treatment taught by Reid is necessarily the same as that claimed because the treatment comprises the same reagents, steps and effects. Differentiation is inherent to the administration based on the noted effects of TGF-α, see in particular Weiss et al., US5,980,885 as set forth below. Thus, the reference teachings anticipate the claimed invention.

11. Claims 1-8, 16 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Weiss et al., 5,980,885, filed June 7, 1995 and issued Nov. 9, 1999.

It is disclosed as is recognized in the art that TGF-α binds the EGF receptor, see in particular p. 2 and Todaro et al., PNAS 77:5258-62, 1980.

Weiss et al., teach administration of TGF-α to brain for the purpose of inducing in vivo proliferation, migration and differentiation of neural and/or glial cells and for treatment of Huntington's, Alzheimer's, Parkinson's and other neurological disorders, see in particular Abstract, column 26, lines 16-26 and Examples 27-30. In addition, the method may be used in areas of demyelination or autoimmune disease such as MS for proliferation of glial schwann, see in particular columns 24-25. The method is also disclosed for use in the replacement of neurons, for example as transplants or grafts, disclosed at column 23. Weiss further teaches that the method may be generically used to replace damaged or missing neurons and/or glia, see in particular Abstract.

As the treatment of Weiss involves administration of TGF-α to the brain and results in the contact of TGF-α, a compound that binds the EGF receptor with neural progenitor cells within the brain, the treatment taught by Weiss is necessarily the same as that claimed because the treatment comprises the same reagents, steps and effects as noted.. Thus, the reference teachings anticipate the claimed invention.

12. Claims 1-7, 16 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Alexi et al., Neuroscience, 78(1):73-86, May 1997.

It is disclosed as is recognized in the art that TGF-α binds the EGF receptor, see in particular p. 2 and Todaro et al., PNAS 77:5258-62, 1980.

Alexi et al., teach lesioning of striatum with quinolinic acid as an animal model of Huntington's disease. In this model, intra striatal injection of TGF-α resulted in protection against the phenotypic degeneration of the striatal cell population in vivo. As the method is used as a treatment of Huntington's brain and comprises contacting the brain at the site of lesion with TGF-α in an amount sufficient to protect against the phenotypic degeneration, the treatment is deemed to inherently provides for proliferation, migration and differentiation of the cells. In particular the sufficient amount is not differentiated from the noted effects in the claim. As the Patent Office lacks sufficient means to determine if in-fact the quantities of the methods as claimed and disclosed are the same, the burden shifts to applicant to distinguish the subject matter claimed from that disclosed. Thus, the reference teachings anticipate the claimed invention.

Status of Claims

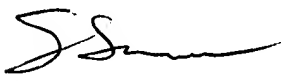
13. No claims are allowed.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The

examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.



Sharon L. Turner, Ph.D.
July 28, 2002